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The Effectiveness of Atrial Fibrillation Special Clinic on Oral Anticoagulants Use for High Risk Atrial Fibrillation Patient Managed in the Community

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Abstract

Background: There are service gaps existed in atrial fibrillation (AF) management in Hong Kong with relatively low utilization of oral anticoagulants. The purpose of this study was to explore the clinical effectiveness of Atrial Fibrillation Special Clinic (AFSC) by evaluating its impact on the oral anticoagulants use and the control of modifiable cardiovascular disease (CVD) risk factors in high risk AF patients.

Method: This was a quasi-experimental, pre-test/post-test study in public primary care clinics. Participants included high risk AF patients with CHA_2DS_2-VASc score ≥2, had been followed up (FU) for one year at 5 AFSCs of Kowloon Central Cluster (KCC) of the Hospital Authority of Hong Kong from 01 August, 2019 to 31 October, 2020. Our primary outcomes were 1) total number of patients agreed for novel oral anticoagulant (NOAC) treatment after recruitment at AFSC, and 2) modifiable CVD risk factors control including blood pressure (BP), Haemoglobin A1c (HbA1c) if diabetic and low-density lipoprotein-c (LDL-c) level, compared at baseline and after one year FU. Our secondary outcomes were drug-related adverse events, major bleeding and non-major bleeding episodes, stroke or systemic embolism events, Accident and Emergency Department attendance or hospitalisation episodes, survival and mortality rates after one year FU.

Results: Among the 299 high risk AF patients included in the study, significant increase in NOAC utilization was observed from 58.5% to 82.6% after FU in AFSC (P <0.001). Concerning the CVD risk factors control, the average diastolic BP level was significantly reduced (P=0.009) and the satisfactory BP control rate in non-DM patients was significantly improved after one year FU (P=0.049). However, the average HbA1c and LDL-c level remained static. The annual incidence rate of ischaemic stroke/systemic embolism was 0.4%, intra-cranial haemorrhage was 0.4%, major bleeding episode was 3.2% and all-cause mortality was 4.3%, all of which were comparable to the literatures.

Conclusion: AFSC is effective in enhancing NOAC use and maintaining optimal modifiable CVD risk factors control among high risk AF patients managed in primary care setting, therefore may reduce AF-associated morbidity and mortality in the long run.

Introduction

Atrial fibrillation (AF) is a common type of cardiac rhythm disorder with uncoordinated atrial electrical activity and motion of the atrial wall [1]. Globally, it was estimated that 33.5 million patients (20.9 million for men; 12.6 million for women) had AF in 2010. The number of new AF cases was estimated to be 4.7 million per year [2], with greater prevalence in elderly and in patients with co-morbidities [3–4]. Locally, AF affects about 1 percent of the population in Hong Kong.

AF is a progressive disease which develops from paroxysmal form through persistent to permanent AF, due to ongoing electrical and structural remodeling of the atria [5–6]. A number of risk factors and predisposing conditions had been identified to be associated with the development and progression of

AF. Apart from the unmodified risk factors such as advancing age, gender, ethnicity and genetic predisposition, the presence of hypertension (HT), diabetes mellitus (DM), obesity, congestive heart failure, myocardial infarction, valvular heart disease, smoking and alcohol consumption are all important modifiable risk factors [7–10]. Early detection and strict control of these modifiable risk factors could effectively prevent the progression of AF. For example, in the ARREST-AF Cohort (Aggressive Risk Factor Reduction Study for Atrial Fibrillation) study, comprehensive risk factor modifications including blood pressure (BP), low-density lipoprotein-c (LDL-c) and haemoglobin A1c (HbA1c) control have significantly improved the arrhythmia free survival by reversing the structural remodeling with improvement in left atrial volume and left ventricular hypertrophy [11].

AF is a cause of significant morbidity and mortality [12–13]. People with AF have five-fold increased risk of stroke than non-AF patients [14], and anticoagulation treatment has been shown to significantly reduce the risk of stroke in AF patients [15]. Therefore, antithrombotic therapy is an integral part of AF management to prevent the thromboembolic events. CHA_2DS_2-VASc score (Congestive heart failure, HT, Age ≥ 75 years [doubled], DM, prior Stroke or transient ischemic attack [doubled], Vascular disease, Age 65–74 years, and Sex category [female]) is a well-validated risk-stratification score for predicting stroke events in patients with AF [16], whereas HAS-BLED scores (Hypertension, Abnormal renal and liver function, Stroke, Bleeding tendency, Labile INRs, Elderly, Drugs or alcohol) provides prediction of bleeding risk [17]. The European Society of Cardiology (ESC) guideline recommends no treatment for patient with CHA_2DS_2-VASc score of 0, whereas oral anticoagulant is indicated for patient with a score ≥ 2 and should be considered for patients with a score of 1. Oral anticoagulants (OAC) currently used are 1) the vitamin K antagonist (VKA) – warfarin, which impairs the synthesis of clotting factors II, VII, IX and X, and 2) novel oral anticoagulants (NOAC), which selectively inhibit only thrombin (dabigatran) or factor Xa (rivaroxaban, apixaban, and edoxaban). Patient with mitral stenosis or artificial heart valves should be treated with VKAs, while NOACs are suitable alternatives for non-valvular AF [18]. Studies have shown that NOACs have similar or better efficacy than warfarin with less risk of bleeding, with no monitoring required and fewer drug and diet interactions [19].

Despite all these evidence, service gaps existed in AF management, and the utilization of OACs for AF managements remained low persistently [20–22]. After the availability of NOACs in the market, the OAC utilization rates in AF patients still varied among different countries. For example, a study in U.S. showed OAC utilization rate among indicated AF patients was 11-78.8% with 0-40.4% using NOAC [23], while a study in China found a total of 35.6% of indicated AF patient had received OAC but only 11.1% of them were using NOAC [24]. Similarly, a local study conducted in hospital setting revealed that only 23% of high risk AF patient had received OACs [25]. However, there is no information on NOAC use among AF cases managed in primary care setting and their cardiovascular disease (CVD) risk factors control. AF Special Clinic (AFSC) was established in the Department of Family Medicine and General Outpatient Clinics (Dept. of FM and GOPCs) of Kowloon Central Cluster (KCC) of Hospital Authority (HA) of Hong Kong in June 2019. The aim of setting up this clinic is to provide holistic and comprehensive management to AF patients in the community. This study tried to explore the clinical effectiveness of

AFSC by evaluating its impact on anticoagulant use and the control of CVD risk factors among high risk AF patents managed in public primary care clinics. We believed that AFSC could help enhance the NOAC utilization and improve the CVD risk factors control, and consequently reduce the incidence of ischaemic stroke and mortality in AF patient in the long run.

Methods

Study design: A quasi-experimental, pre-test/post-test design

Definition of different risks of AF in this study

According to the AF management guideline from European Society of Cardiology [26], CHA_2DS_2-VASc score (**Table 1**) should be calculated for all AF cases to stratify their stroke risk. If the patient has a CHA_2DS_2-VASc score ≥ 2, he/she is considered as a 'high risk' AF patient and OAC is recommended. If the patient is 'low risk' with the CHA_2DS_2-VASc score being 0 in males or 1 in females, no OAC therapy is recommended. In males with 1 stroke risk factor (i.e. CHA_2DS_2-VASc score = 1), OAC may be considered, and people's value and preference should be considered [27].

Study subjects

Inclusion criteria:

High risk AF patients coded by International Classification of Primary Care 2nd version (ICPC-2)-code of "K78" (atrial fibrillation), whose CHA_2DS_2-VASc score was ≥ 2, had been FU for one year at 5 AFSCs of KCC of the HA of Hong Kong from 01 August, 2019 to 31 October, 2020.

Exclusion criteria:

1. AF Patients who have contraindications to NOACs therapy, they are:

A) Absolute contraindications

- Potential bleeding lesions
- Active peptic ulcer, aneurysm, and preoperative retinopathy
- Recent organ biopsy
- Recent trauma or surgery to the head, orbit or spine
- Recent stroke
- Confirmed intracranial bleed
- Uncontrolled hypertension
- Infective endocarditis

B) Relative contraindications

- History of gastrointestinal bleeding
- Liver disease
- Renal failure on dialysis
- Alcoholism
- Mental impairment
- Thrombocytopenia
- Coagulation disorders
- Interacting drugs, i.e. Non-steroidal anti-inflammatory drugs
- Poor concordance

C) Special contraindications

1. Mechanical prosthetic valve or moderate to severe mitral stenosis
2. Pregnancy
3. Child-Pugh category C hepatic insufficiency
4. Severe renal impairment

- estimated glomerular filtration rate < 30 mL/min/1.73 m^2 for dabigatran
- estimated glomerular filtration rate < 15 mL/min/1.73 m^2 for factor Xa inhibitors

1. Patients defaulted AFSC follow-up
2. Patients FU in Specialist Outpatient Clinic (SOPC) for management of AF
3. AF Patients certified death during the study period
4. AF patients with incomplete data

Case recruitment at AFSC

Totally there are 5 AFSCs in the Dept. of FM and GOPCs of KCC in HA. They located at Yau Ma Tei Jockey Club GOPC (YMTJC GOPC), Shun Tak Fraternal association Leung Kau Kui Clinic (FALKK GOPC), Central Kowloon Health Centre (CKHC), East Kowloon GOPC (EK GOPC) and Our Lady of Maryknoll Hospital Family Medicine Clinic (OLMH FMC). AF patients encountered in any GOPC of KCC, if CHA_2DS_2-VASc score was ≥ 2, would be referred to the closest AFSC for anticoagulation counselling and management since 01 August, 2019. A run-in period of about 3 months was allowed for case recruitment.

Management at AFSC

The attending doctors at AFSCs were experienced FM specialists who had received training on AF management via standardized educational talk. Patient's epidemiological characteristics such as age, gender, smoking status, drinking status, co-morbidities including HT, DM and CHF, past history of ischaemic heart disease (IHD), stroke/transient ischaemic attack (TIA) or intra-cranial haemorrhage (ICH) and type of AF (non-valvular, which confirmed by physical examination and previous Echocardiography

result) were reviewed. CHA_2DS_2-VASc score [16] and HAS-BLED score were calculated and documented too. Baseline blood tests including complete blood picture, clotting profile, serum creatinine, alanine transaminase, glucose, HbA1c and lipid profile were checked. The estimated glomerular filtration rate (eGFR) was calculated by using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [28], i.e.

$141 \times \min(S_{cr}/\kappa, 1)^{\alpha} \times \max(S_{cr}/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018$ [if female] x 1.159 [if African American]
where:

S_{cr} is serum in mg/dL,

κ is 0.7 for females and 0.9 for males,

α is -0.329 for females and − 0.411 for males,

min indicates the minimum of Scr/K or 1, and

max indicates the maximum of Scr/K or 1

With the introduction of NOACs to the Drug Formulary of GOPCs in HA in July 2019, AF patients whose CHA_2DS_2-VASc score is ≥ 5 could get the NOACs for free in HA Pharmacy. For those whose CHA_2DS_2-VASc score is between 2–4, the patients had to purchase the NOAC as self-financed item (SFI) from community pharmacy. Two types of NOACs were available in AFSCs in KCC, they were Dabigatran and Apixaban. Patient could also choose other NOACs as SFI. The potential risks and benefits of anticoagulation therapy had been thoroughly discussed to the patients by the attending FM doctor. Updated international guidelines and appropriate local therapeutic instructions were also available on our department website.

At each follow-up (FU) visit at AFSC, patient's medication adherence and adverse effects were assessed. Blood test results, Accident and Emergency Department (AED) admission or hospitalizations were also documented. The aim, procedures and nature of study had been explained by the principal investigator or the research assistant. Written consent had been obtained from each subject who agreed to participate in the study. All patients were informed that they would be free to withdraw at any time during the study.

Data collection

The list of patients fulfilling the inclusion criteria were retrieved from the Clinical Data Analysis and Reporting System (CDARS) of HA. Patient's age, gender, smoking status and alcohol status were retrieved from the Clinical Management System (CMS) of HA. Their clinic BP level on the first AFSC attendance and after one year FU were collected. The biochemical parameters including HbA1c and LDL-c level before recruitment of AFSC and after one year FU were compared. Their AED attendance, hospitalization records and mortality data during the study period were also retrieved from the CMS.

Outcome measures

The *primary outcomes* include the followings:

1. Total number patients agreed for NOAC treatment after recruitment in AFSC, and
2. Modifiable CVD risk factors control, in terms of BP, HbA1c and LDL-c level, were compared at baseline and after one year FU.

- For HT patients without DM, BP < 140/90mmHg was defined as satisfactory control
- For HT patients with DM, BP < 130/80mmHg was defined as satisfactory control
- For DM patient, HbA1c < 7% was defined as satisfactory control
- For patients without history of CVD, LDL-c < 2.6mmol/L was defined as satisfactory lipid control
- For patients with history of CVD, LDL-c < 1.8mmol/L was defined as satisfactory lipid control

The *secondary outcomes* after one year FU include the followings:

1. Drug-related adverse events
2. Major bleeding and non-major bleeding episodes
3. Stroke or systemic embolism events
4. AED attendance or hospitalisation episodes
5. Survival and mortality rates

Major bleeding episodes (MBE) were defined per the International Society on Thrombosis and Hemostasis (ISTH) criteria as one of the following [29]:

- Fatal bleeding, and/or
- Symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome, and/or
- Clinically overt bleeding with a decrease in the haemoglobin level of $\geq$ 2g/dl or transfusion of $\geq$ 2 units of packed red cells.

Any reported bleeding episode that did not meet the criteria for major bleeding was defined as a non-major bleeding episode (NMBE).

Termination criteria

The whole research plan would be terminated for following circumstances:

1. Presence of serious adverse effect related to intervention with supportive evidence;
2. Completion of all FU assessment

Sample size calculation

A local AF screening done among 1,581 elderly aged 65 or above in the community with the use of a handheld ECG device between 2013 and 2014 found that around 7% of elderly had AF [30]. Another local

study revealed that among patients with AF and a high risk of stroke, only 23% received OACs [25]. Based on these findings, and considering the comprehensive team-based approach at AFSC, we assumed that a much higher proportion of high risk AF patients, i.e. up to 50%, would receive NOACs treatment after being recruited to FU at AFSC. Based on level of significance (α = 0.05), the power of the test (β = 0.2 power of the test 80%) and the effect size (*d* = 0.5), the minimum sample size is **283**. To allow the room for case exclusion and assumed a 15% dropout rate, **325** people had been recruited.

Statistical analysis

All data were entered and analyzed using computer software (Windows version 23.0; SPSS Inc, Chicago [IL], US). Patient characteristics were described using proportions for categorical variables and means with standard deviations for continuous variables. Baseline characteristics were presented as percentages for categorical variables and mean ± standard deviation (SD) for continuous variables. Chi-square test was used for univariate comparisons of categorical variables between groups. Student's t test was used for continuous variables. All statistical tests are two sided, and a P value of less than 0.05 is considered statistically significant.

Ethical approval

The study was approved by Research Ethics Committee of Kowloon Central Cluster of Hospital Authority of Hong Kong, the approval number was KC/KE-19-0143/ER-3.

Results

Totally 325 high risk AF patients had attended AFSC during the study period, among which 194 patients had already taken NOAC whereas 131 patients did not. After thorough discussion with the attending FM specialist doctor in AFSC, 72 patients of those who did not take NOAC before agreed to start NOAC, whereas only 59 patients still declined it. Among the NOAC group, totally 19 patients were excluded after one-year FU, with 6 having FU in CGAT, 2 defaulted FU and 11 patients died. In the non-NOAC group, 7 patients were excluded, with 2 defaulted FU, 3 cases with incomplete data and 2 patients died.

Among the 11 cases who died in the NOAC group, 1 patient died of ICH occurred at 6 months after initiation of NOAC with incidence rate 0.4% and 1 patient died of ischaemic stroke who had already taken NOAC prior attending AFSC, also with incidence rate 0.4%. Causes of the other 9 deaths were non-NOAC related including pneumonia, MI and cancer. The one-year all-cause mortality rate in NOAC group was 4.3%. 6 cases moved to old-aged home and FU by Community Geriatric Assessment Team (CGAT) subsequently. The 2 defaulted FU cases had no admission history due to NOAC related complications or side effects from the CMS.

As to the 2 cases died in the non-NOAC group, both died of pneumonia, with one-year all-cause mortality rate being 3.7%, which is not significant (P=0.85) compared with the NOAC group.

After case exclusion, total 299 cases including 247 patients on NOAC and 52 patients declined NOAC were included in the final data analysis. The flowchart of case recruitment for this study was summarized in **Figure 1**.

Among the 299 patients included in the data analysis, their mean age was 82.5±7.4 years, with 87% were over 75 years, 12% were 65 to 74 years old, and only 1% were younger than 65 years old. 200 (66.9%) were female patients, whereas 99 (33.1%) were male. Majority of patients were non-smoker and non-drinker with 82.3% and 97.6% respectively. The mean CHA_2DS_2-VASc score was 5.38 (±0.95), with 90.3% patients with CHA_2DS_2-VASc score ≥5 and 9.7% with CHA_2DS_2-VASc score 2-4, and mean HAS-BLED score was 1.70 (±0.69).

Regarding the AF related risk factors, there were 288 (96.3%) patients with HT, 161 (53.8%) patients with DM, 52 (17.4%) patients with CHF, 49 (16.4%) patients with IHD and 150 (50.2%) patients with previous history of stroke/TIA. 143 (47.8%) patients with satisfactory baseline renal function of eGFR greater than 60 mL/min/1.73 m^2, 150 (50.2%) patients had renal impairment of eGFR 30-59 mL/min/1.73 m^2 and 6 (2%) had severe renal impairment of eGFR less than 29 mL/min/1.73 m^2. **Table 2** summarized the demographic characteristics of patients FU at AFSC.

Primary outcomes

AF patients agreed for NOAC use after visiting AFSC showed statistically significant increase from 58.5% to 82.6% (P<0.001) as in **Table 3.** Among them, 105 (35.1%) patients were prescribed dabigatran, 139 (46.5%) were on apixaban, and 3 (1%) were on rivaroxaban.

Table 4 summarized modifiable CVD risk factors control in patients on NOAC at baseline and after one year FU. Among the 236 patients with HT, their average systolic BP (SBP) was 128.1 (±13.3) mmHg and diastolic BP (DBP) was 71.0 (±11.5) mmHg. After one year FU, SBP remained static at 126.9 (±10.9) mmHg (P=0.30), and the DBP was statistically significantly decreased to 68.3 (±10.6) mmHg (P=0.009). For hypertensive AF patients without DM, 81.7% (n=89) patients got satisfactory BP control and the rate was further increased to 90.8% (n=99) after one year FU (P=0.049). In hypertensive patients with DM, the BP control rate remained static after one year FU (P=0.52).

Among the 130 AF patients comorbid with DM, their average HbA1c level (6.68% versus 6.65%) and satisfactory glycaemic control rate remained static from baseline to one year after FU (P=0.71 and P=0.27 respectively). The average LDL-c level at baseline and one year after FU had been comparable too (1.70 mmol/L versus 1.62mmol/L, P=0.08) and subgroup analysis showed that the LDL-c control rate remained static in both with or without history of CVD group, P=0.05 and P=0.72 respectively.

Secondary outcomes

Table 5 compared secondary outcomes of patients on NOAC during the study period. Upon completion of 12 months FU, total 12 bleeding episodes were observed, which 8 were MBE at a rate of 3.2%/year, 4

(1.6%/year) were NMBE.

The 8 patients with MBE were due to gastrointestinal (GI) bleeding, within which 3 patients was put on NOAC <3 months (1.2%), 2 patients <6 months (0.8%), 2 patients <12 months (0.8%) and 1 patient was put on NOAC >1 year (0.4%). In the 4 patients suffered from NMBE, 3 patients reported haematuria and 1 patient had haemoptysis.

We also observed total 65 AED attendance/ hospitalisation events, incidence rate 26.3%. Causes of admission included pneumonia, CHF, MI, atypical chest pain, syncope, fall with or without fracture and cancer. 2 patients complained of non-specific general discomfort, tiredness and muscle discomfort after taking NOAC and they consequently declined to use NOAC. There was no serious adverse effect observed.

Discussion

Although OAC have shown to be effective for stroke prevention among AF patients, its utilization rate was only 19.7% to 23% among indicated AF patients managed in secondary care setting according to local study findings [25,31]. Benefit of OAC balancing against the risk of serious bleeding accounted for one of the important factors affecting the use of OAC. Overestimation of the bleeding risk and disadvantage associated with advanced age, such as fall risk, are other well-known obstacles [32]. Furthermore, lack of reversal agents may also affect patients' decision of using NOAC [33]. In our study, there was a significantly increase in NOAC utilization after enrolled in AFSC, with 82.6% of them agreed to use NOAC. This rate was significantly higher than those reported in the literature. The reasons contributing to this satisfactory utilization rate were multi-factorial. Firstly, most of the AF cases referred to have FU at AFSC were of high risk or very high risk groups, therefore these group of patients were more willing to try NOAC after discussion with the doctor. Secondly, with the availability of NOAC including Apixaban and Dabigatran at AFSCs of HA since March 2019 and implementation of HA policy that AF patients whose CHA_2DS_2-VASc score ≥ 5 can be provided with NOAC for free have helped eased the financial difficulty of many high risk AF patients, many of them otherwise have to purchase the NOAC as SFI before this exercise. Based on these positive results, we would like to propose to Hong Kong government that free NOAC should be provided for all high risk AF patients whose CHA_2DS_2-VASc score is ≥ 2, although balancing the use of public resources and costs was also important. Thirdly, the attending doctors at AFSC are experienced FM specialists who were more skillful in AF management. They had provided a comprehensive assessment of AF patient's background characteristics and comorbidities, and have done a thorough explanation and education of NOAC use to the AF patients.

Recent years, more evidences supported an integrated multidisciplinary approach with treatments and management of modifiable CVD risk factors and underlying conditions could slow progression and improves the outcomes of AF [34]. Greater reduction in BP and better glycemic control and lipid profiles were associated with decreased AF frequency, duration and symptoms [11]. AFSC aimed to provide comprehensive care with treatment and tailored information about advice and education on risk factors

management to AF patients by targeting their underlying medical conditions. Our study showed a reduction of average diastolic BP and more non-DM hypertensive patients with satisfied BP control after being FU in AFSC. Although HbA1c and LDL-c level showed no significant change after one year FU, their satisfactory control rate remained consistently high from the baseline till one year FU. Therefore, AFSC could help AF patients maintain optimal CVD risk factors control, which may subsequently prevent the progression of AF.

The safety and efficacy of NOAC for general population have been well demonstrated by different clinical trials recent years. For example, a retrospective observational study found both apixaban and dabigatran had lower incidences of ischaemic stroke 1.3-1.4% and MBE 3.6% when compared to warfarin [35]. Our study showed comparable result with the literature with annual MBE incidence being 3.2%. The lower incidence of ischaemic stroke (0.4%) of our study might be due to the strict and satisfactory CVD risk factor control among AF patients managed at AFSC. Concerning the mortality rate, our study showed that the all-cause mortality rate of NOAC use after one year was 4.3%, which was also consistent with findings from UK which showed an all-cause mortality rate of 4% in a large cohort study [36]. Therefore, the use of NOAC in AFSC was proved to be safe and effective with comparable stroke risk, bleeding risk and mortality rate to findings in the literatures.

Strength of the study

This study is the first local study to assess the anticoagulation use and the CVD risk factor control among high risk AF patients managed in public primary care clinics, therefore have provided important background information on anticoagulation use in the public primary care setting and help to identify service gaps and direct future service enhancement strategies. In addition, all parameters including BP, HbA1c and LDL level were based on data of objective assessment retrieved from the CMS, thus recall bias or data entry bias had been minimized.

Limitations of the study

There are several limitations of the study. First, as this study was done in public general out-patient clinics of a single cluster in HA, selection bias might exist. The result from this study may not be applicable to private sector or secondary care setting. In addition, most of the AF cases assessed at AFSC had a higher CHA2DS2-VASc score of ≥ 5 (90.3%) due to HA Drug Formulary free dispensing arrangement for such very high risk AF patients, which have further confounded the findings of the study. The much higher NOAC utilization rate achieved at the AFSCs may not be comparable to other settings where most AF patients were having a lower CHA_2DS_2-VASc score of 2-4. Second, due to the intrinsic limitations of the study design, the quasi experimental design without a control group, causal temporal relationship could be established. Third, the one year FU duration may not be long enough to assess the long-term effect of NOAC use among AF patients. In this regard, a randomized-control study design with a control group, and longer FU study (more than one year) would help evaluate the efficacy of AFSC more

comprehensively. Furthermore, study of underlying obstacles of OAC prescription and subgroup analysis for safety and effectiveness of NOAC may help physicians make the clinical decision sensibly.

Conclusion

AFSC is effective in enhancing NOAC use and maintaining optimal modifiable CVD risk factors control among high risk AF patients managed in public primary care clinics. With a much higher rate of anticoagulant use and better CVD risk factor control, it is postulated that AF-associated morbidities and mortality will be reduced in the long run.

Abbreviations

AED: Accident and Emergency Department; AF: Atrial Fibrillation; BP: Blood Pressure; CMS: Clinical Management System; CVD: cardiovascular disease; DM: Diabetes Mellitus; DBP: Diastolic BP; eGFR: Estimated Glomerular Filtration Rate; FU: Follow-up; HbA1c: Haemoglobin A1c; HA: Hospital Authority; HT: Hypertension; ICH: Intra-Cranial Haemorrhage; IHD: Ischaemic Heart Disease; KCC: Kowloon Central Cluster; LDL-c: Low-Density Lipoprotein-c; NOAC: novel oral anticoagulant; OAC: Oral anticoagulant; SFI: Self-Financed Item; SOPC: Specialist Outpatient Clinic; SBP: systolic BP; TIA: Transient Ischaemic Attack; VKA: Vitamin K Antagonist;

Declarations

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Author’s contributions

KML, CXRC, designed the study. KML was involved with data acquisition. All authors contributed to data analysis and interpretation. KML, CXRC conducted the literature review, wrote the first drafts and the final versions of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

Ethics approval and consent to participate

The study was approved by the Research Ethics Committee of Kowloon Central Cluster of Hospital Authority of Hong Kong in August 2019, the approval number was KC/KE-19-0143/ER-3. Informed consent was obtained from all subjects and/or their legal guardian(s) agreed to participate in the study. All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1 CHA_2DS_2-VASc score

Letter	Risk factor	Score
C	Congestive heart failure	1
H	Hypertension	1
A_2	Age ≥ 75	2
D	Diabetes mellitus	1
S_2	Stroke/TIA/thrombo-embolism	2
V	Vascular disease*	1
A	Age 65-74	1
S	Sex category (i.e. female sex)	1
	Maximum score	9

Congestive heart failure means signs/symptoms of heart failure confirmed with objective evidence of cardiac dysfunction. Hypertension includes the patients with resting BP>140/90mmHg on at least 2 occasions or with current antihypertensive medication. *Prior myocardial infarction, peripheral artery disease, aortic plaque. TIA: transient ischaemic attack

Table 2 Demographics characteristics of patients at AFSC

Characteristics	Total Number (n=299)
Age (years)	82.5 (±7.4)
<=64 years	3 (1.0)
65-74years	36 (12.0)
>=75 years	260 (87.0)
Gender	
Female	200 (66.9)
Male	99 (33.1)
Smoking status	
Non-smoker	246 (82.3)
Ex-smoker	44 (14.7)
Smoker	9 (3.0)
Drinking status	
Non-drinker	292 (97.6)
Ex-drinker	2 (0.7)
Drinker	3 (1.0)
Social-drinker	2 (0.7)
Co-morbidities	
Hypertension	288 (96.3)
Diabetes mellitus	161 (53.8)
Congestive heart failure	52 (17.4)
Ischaemic heart disease	49 (16.4)
Previous stroke/TIA	150 (50.2)
Previous intra-cranial haemorrhage	3 (1.0)
Renal function	
eGFR ≥60 mL/min/1.73 m^2	143 (47.8)
eGFR 30-59 mL/min/1.73 m^2	150 (50.2)
eGFR <29 mL/min/1.73 m^2	6 (2.0)
Scores	

CHA_2DS_2-VASc score	5.38 (±0.95)
0-1	0
2-4	29 (9.7)
≥5	270 (90.3)
HAS-BLED score	1.70 (±0.69)
NOAC at baseline	175 (58.5)
Dabigatran	90 (30.1)
Apixaban	52 (17.4)
Rivaroxaban	25 (8.4)
Warfarin	8 (2.7)
non-NOAC at baseline	124 (41.5)
Aspirin	115 (38.5)
Plavix	3 (1.0)
None	6 (2.0)
Data are shown as mean (±standard deviation) or number of cases (%)	

Table 3 Comparison of NOACs utilization in AF patients before and after recruited at AFSC (n=299)

Variables	Before AFSC	After AFSC	P-value#
NOAC	175 (58.5)	247 (82.6)	**<0.001**
CHA_2DS_2-VASc score 2-4	11 (3.7)	18 (6.0)	
CHA_2DS_2-VASc score ≥5	164 (54.8)	229 (76.6)	
Dabigatran	90 (30.1)	105 (35.1)	
Apixaban	52 (17.4)	139 (46.5)	
Rivaroxaban	25 (8.4)	3 (1.0)	
Warfarin	8 (2.7)	0	
non-NOAC	124 (41.5)	52 (17.4)	**<0.001**
CHA_2DS_2-VASc score 2-4	18 (6.0)	11 (3.7)	
CHA_2DS_2-VASc score ≥5	106 (35.5)	41 (13.7)	
Aspirin	115 (38.5)	36 (12.0)	
Plavix	3 (1.0)	3 (1.0)	
None	6 (2.0)	13 (4.3)	
Data are shown as number of patients (%)			
# For comparison of AF patients before and after recruited at AFSC by Chi-squared test			

Table 4 Modifiable CVD risk factor control in NOAC group at baseline and after one year FU

Variables	At baseline	After 12 months	P-value§
Hypertension (n=236)			
SBP mmHg	128.1 (±13.3)	126.9 (±10.9)	0.30
DBP mmHg	71.0 (±11.5)	68.3 (±10.6)	***0.009***
1) without DM (n=109)			
Number of patients with satisfactory control	89 (81.7)	99 (90.8)	***0.049***
2) with DM (n=127)			
Number of patients with satisfactory control	76 (59.8)	81 (63.8)	0.52
Diabetes mellitus (n=130)			
HbA1c %	6.68 (±0.71)	6.65 (±0.77)	0.71
Number of patients with satisfactory control	89 (68.5)	97 (74.6)	0.27
Hyperlipidemia (n=247)			
LDL-c mmol/L	1.70 (±0.55)	1.62 (±0.52)	0.08
1) without history of CVD (n=82)			
Number of patients with satisfactory control	77 (93.9)	79 (96.3)	0.72
2) with history of CVD (n=165)			
Number of patients with satisfactory control	109 (66.1)	125 (75.8)	0.05
Data are shown as mean (±standard deviation) and number of patients (%);			

Table 5 Secondary outcomes of patients on NOAC during the study period

Variables	Total number (n=247)
Major bleeding events	8 (3.2)
Duration of taking oral anticoagulants	
less than 3 months	3 (1.2)
3-6 months	2 (0.8)
6-12 months	2 (0.8)
more than 12 months	1 (0.4)
Causes of major bleeding	
GI bleeding	8
Non-major bleeding events	4 (1.6)
Haematuria	3
Haemoptysis	1
AED attendance/hospitalization	65 (26.3)
Data are shown as number of patients (%)	

Figures

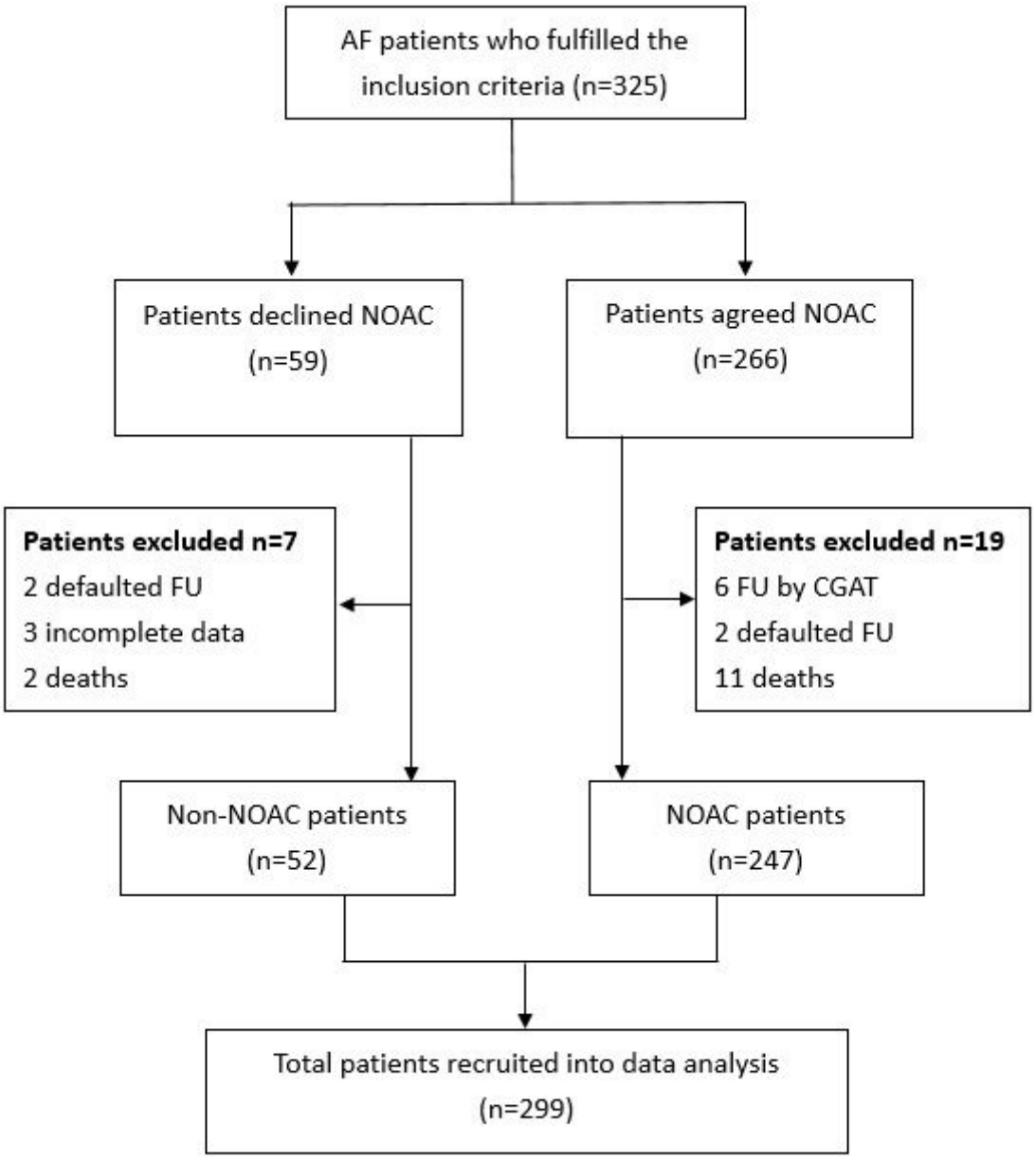

Figure 1

Flow chart of case recruitment at AFSC during the study period.

AFSC, atrial fibrillation special clinic; SOPC, specialist out-patient clinic; NOAC, novel oral anticoagulant

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- NOAC247characteristics.sav
- NOAC247modifiableriskfactorsbeforeandafter12months.sav

- NOACDMbeforeandafter12months.sav
- NOACHTwithDMbeforeandafter12months.sav
- NOACHTwithoutDMbeforeandafter12months.sav
- NOAClipidbeforeandafter12months.sav
- NOAClipidwithCVDbeforeandafter12months.sav
- NOAClipidwithoutCVDbeforeandafter12months.sav
- TotalNOACnonNOAC299characteristics.sav